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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,257	BERTELLI ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *3,6,8-21 and 23-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7 and 22* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/20/03 & 8/29/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. The amendment of 29 August 2003 in the disclosure have been entered in full.

Election/Restrictions

2. Applicant's election without traverse of Group I, claims 1, 2, 4, 5, 7 and 22, drawn to a method for the screening of ligands binding a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$-1 subunit, in the reply filed on July 27, 2006 is acknowledged.

3. Claims 3, 6, 8-21 and 23-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 27, 2006.

4. Claims 1, 2, 4, 5, 7 and 22 drawn to a method for the screening of ligands binding a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$-1 subunit using a flashplate assay, are under consideration in the instant application. Claims 3, 6, 8 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected species, there being no allowable generic or linking claim.

5. Applicant's election of "flashplate assay" as the species and SEQ ID NO: 33 as the elected sequence from the secondary restriction requirement will be considered for examination. Upon consideration, the requirement of species for the 'peptide epitope tag type' and 'ligand' is withdrawn.

6. Applicant's request for examination of SEQ ID NO: 44 is not found persuasive. Applicant cites MPEP § 2434 in requesting that an additional sequence (SEQ ID NO: 44) be searched. However, MPEP § 2434 allows for but does not require additional searches, and further is directed only to claims for sequences, not methods of using same, which require additional considerations.

Specification

7. The disclosure is objected to because of the following informalities:

A) An updated status of the parent patent application should be included in the first sentence of the specification. A statement reading, "This application is a continuation of U.S. Serial No. 09/397,549, filed September 16, 1999, 'now abandoned'," should be entered. Appropriate correction is required.

B) The abstract of the disclosure is objected to because of the lack of proper and sufficient content to support the claimed invention.

The abstract of the disclosure is objected to because it refers to clearly speculative applications of the claimed invention. A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is

new in the art to which the invention pertains. Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.
(See MPEP § 608.01(b)).

A new abstract in compliance with M.P.E.P. 608.01(b) is required.

Claim Objections

8. Claim 5 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claims. See MPEP § 608.01(n). Accordingly, the claim 5 is not been further treated on the merits.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 2, 4, 7 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening of ligands and biologically active products that bind a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$-1 subunit of SEQ ID NO:

37 using a flashplate assay, does not reasonably provide enablement for screening of ligands that bind to all species of $\alpha_2\delta$-1 subunit polypeptides having 80% or more amino-acid identity with the polypeptides comprising amino acids 1 to between 1008 and 1087 amino acids of SEQ ID NO: 33 as claimed as in claim 7, and those of no defined relationship to SEQ ID NO: 33 as claimed in claims 1 and 2 and claims depending therefrom. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

10. The claims are directed to a method of screening of ligands and biologically active compounds that bind to a soluble secreted $\alpha_2\delta$-1 subunit polypeptide, or having a minimum of 80% identity comprising amino acid 1 to between 1008 and 1087 amino acids of SEQ ID NO: 33. The claims further recite that the screening is conducted by measuring the binding of the labeled compound to the secreted soluble $\alpha_2\delta$-1 subunit polypeptide using the flashplate assay.

11. The specification of the instant application teaches a secreted soluble $\alpha_2\delta$-1 subunit polypeptide of voltage-dependent calcium channel $\alpha_2\delta$ subunit polypeptide that binds to gabapentin (page 1, lines 5-7; page 11, lines 8-14). The specification also teaches that the amino acids close to the C-terminal region of the $\alpha_2\delta$-1 subunit polypeptide are required for binding (page 2, lines 8-9). Furthermore, the specification teaches that

mutant $\alpha_2\delta$-1 proteins that are expressed using cDNA deletion mutants wherein the nucleotide sequences encoding amino acids 985-1091 of SEQ ID NO: 33 have been excised, possibly retain the soluble characteristics as well as the gabapentin binding properties (page 13, lines 5-16). The specification further demonstrates the gabapentin binding assay using a $\alpha_2\delta$-1 deletion mutant of SEQ ID NO: 37 (1069 amino acid peptide) using the flashplate technique (pages 30-31, 34-38, examples 7, 11, figures 3-8). However, the specification does not teach any methods or working examples to indicate that all possible $\alpha_2\delta$-1 subunit polypeptides having at least 80% homology with the polypeptides comprising from amino acid 1 to between amino acids1008 and 1087 of SEQ ID NO: 33 will be useful in the method for screening of "ligands" by measuring binding activity of the subunit. Undue experimentation would be required of the skilled artisan to determine such. The specification does not teach the specific polypeptide domains necessary for preserving the soluble and binding characteristics of $\alpha_2\delta$-1subunit polypeptide. Furthermore, the specification does not teach functional or structural characteristics of the various mutant proteins with regard to ligands recited in the claims other than the polypeptide comprising amino acid sequence of SEQ ID NO: 37 and measuring gabapentin binding. Thus, undue experimentation would be required of the skilled artisan to identify the precise structural characteristics of $\alpha_2\delta$-1 subunit proteins retaining the soluble properties and ligand binding characteristics.

12. Relevant literature states that $\alpha_2\delta$-1 subunit, previously called $\alpha_2\delta$, is a voltage-dependent calcium channel (VDCC) protein, that is membrane bound and widely expressed in the brain (Publication No. US 20050059804, column 1, para 0005; Hofmann et al. Rev of Physiol Biochem and Pharmacol, Vol 139: 33-87, 1999, see page 43; Klugbauer et al. Jour Neuroscience, 19: 684-691, 1999). The art also demonstrates that deletion mutants of the $\alpha_2\delta$ subunit results in increased gabapentin binding activity (Brown and Jee, J Biol Chem 273: 25458-25465, 1998). However, it is not even clear from the relevant prior and post-filing date literature as to what specific regions of the $\alpha_2\delta$-1 subunit sequence or the maximum length of the sequences are essential for biological activity. Thus, undue experimentation would be required of the skilled artisan to identify the precise structural characteristics of $\alpha_2\delta$-1 subunit polypeptides that could be retain soluble characteristics and increased ligand binding properties.

13. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions

directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the $\alpha_2\delta$-1 subunit proteins which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

14. Due to the large quantity of experimentation necessary to generate the infinite number of $\alpha_2\delta$-1 subunit polypeptides recited in the claim that would be soluble and screen the same for binding activity; the lack of direction/guidance presented in the specification regarding the same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function; and the breadth of the claims which fail to recite any structural or functional limitations - undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph- Written Description

15. Claims 1, 2, 4, 7 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

16. Claims 1, 2, 4, 7 and 22 are directed to a method of screening of ligands and biologically active compounds that bind to a soluble secreted $\alpha_2\delta$-1 subunit polypeptide, or a peptide having a minimum of 80% identity comprising amino acid 1 to between 1008 and 1087 amino acids of SEQ

ID NO: 33. The claims further recite that the screening is conducted by measuring the binding of the labeled compound to the secreted soluble $\alpha_2\delta$-1 subunit polypeptide. The claims require that the $\alpha_2\delta$-1 subunit polypeptide sequences generated as stated above are soluble secreted proteins and possess improved ligand binding property, however, the claims do not require that the polypeptide sequences possess any particular conserved structure, or other disclosed distinguishing feature.

17. The specification of the instant application teaches a secreted soluble $\alpha_2\delta$-1 subunit polypeptide of voltage-dependent calcium channel $\alpha_2\delta$ subunit polypeptide that binds to gabapentin (page 1, lines 5-7; page 11, lines 8-14). The specification also teaches that the amino acids close to the C-terminal region of the $\alpha_2\delta$-1 subunit polypeptide are required for binding (page 2, lines 8-9). Furthermore, the specification teaches that mutant $\alpha_2\delta$-1 proteins that are expressed using cDNA deletion mutants, wherein the nucleotide sequences encoding amino acids 985-1091 of SEQ ID NO: 33 have been excised, possibly retain the soluble characteristics as well as the gabapentin binding properties (page 13, lines 5-16). The specification further demonstrates gabapentin binding to a $\alpha_2\delta$-1 deletion mutant of SEQ ID NO: 37 (1069 amino acid peptide) using the flashplate assay (pages 30-31, 34-38, examples 7, 11, figures 3-8). However, the specification does not identify the specific $\alpha_2\delta$-1 subunit sequence having at least 80% identity to amino acids 1 to between 1008

and 1087 of SEQ ID NO: 33 or the maximum length of the sequences essential for ligand binding activity.

18. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The specification has not shown a relationship between the structure, function, or properties of the claimed genus of polypeptides. However, in this case, the only factor present in the claim is a recitation of binding activity. There is not even identification of any particular portion of the $\alpha_2\delta$-1 subunit polypeptide structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The brief description in the specification of one $\alpha_2\delta$-1 subunit polypeptide (SEQ ID NO: 37) is not adequate written description of an entire genus of functionally equivalent polypeptides, which incorporate all fragments, and mutants of $\alpha_2\delta$-1 subunit polypeptide.

19. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the*

invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

20. With the exception of the $\alpha_2\delta$-1 subunit polypeptide sequences referred to above (SEQ ID NO: 37), the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or production. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The *polypeptide itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

21. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

22. Therefore, only the $\alpha_2\delta$-1 subunit polypeptide comprising the amino acid sequence of SEQ ID NO: 37, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written

description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Double Patenting

Statutory

23. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

24. A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

25. Claim 1 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of co-pending U.S. Application No. 11/114,581. This is a double patenting rejection.

Non-Statutory-Provisional

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998);

In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

27. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

28. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

29. Claims 2, 4 and 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 11/114,581. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a method of screening ligands or products by contacting a secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptide with a ligand and a labeled compound that binds to the $\alpha_2\delta$-1 subunit polypeptide, and measuring the level of binding using a flashplate assay. The claims of the 11/114,581 application recite the method of screening of ligands, which bind to $\alpha_2\delta$-1 subunit polypeptide in a flashplate well, while the claims in the instant case recite the screening of biologically active products by measuring the binding of the products to $\alpha_2\delta$-1 subunit polypeptide using a flashplate assay technique. The claims of the '581 application recite the use of 'any' secreted soluble recombinant $\alpha_2\delta$-1 subunit polypeptide, while

claims 2, 4 and 22 of the instant application similarly recite the use of 'any' secreted soluble recombinant $\alpha_2\delta$-1 subunit polypeptide. Claim 22 of the instant case recites the screening assay temperature between 1°C and 30°C, whereas the claims of '581 do not recite an assay temperature. However, this limitation is inherent, because the specification of '581 discloses that the flashplate assay temperature should be between 1°C and 30°C (see page 12, line13). Additionally, optimization within prior art conditions or through routine experimentation is obvious to one skilled in the art. As stated in MPEP 2144.05:

"The differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages". *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382; Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 UDPQ2d 1843 (Fed. Cir.).*

30. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Non-Statutory

31. Claims 1, 2, 4 and 22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2 of U.S. Patent No. 6,958,218. Although the conflicting claims are not identical, they are not patentably distinct from each other because

both sets of claims are directed to a method of screening ligands or products by contacting a secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptide to a ligand along with a labeled compound that binds to the $\alpha_2\delta$-1 subunit polypeptide and measuring the level of binding using a flashplate assay. **(I)** The only difference between claim 1 of the '218 patent and claim 2 of the instant application is that claim 1 of the '218 patent recites the method of screening of ligands that bind to secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptides, while claim 2 of the instant application recites a method for the screening of biologically active products using the same steps. **(II)** The only difference between claim 2 of the '218 patent and claim 4 of the instant application is that claim 2 of the '218 patent recites a method for screening of ligands by measuring the levels of binding to a secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptides, wherein the binding occurs in the well of a flashplate, while claim 4 of the instant application recites the method of measuring the level of binding to a secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptide using the flashplate assay method. **(III)** The patented species claim 1 of '218, which recite a method of screening of ligands by contacting secreted soluble recombinant calcium channel $\alpha_2\delta$-1 subunit polypeptides consisting of SEQ ID NOs: 13, 14 and 15, with a ligand and a labeled compound, render obvious pending genus claim 1 of instant application of a method of screening of ligands by contacting any secreted soluble recombinant calcium channel $\alpha_2\delta$-1

subunit polypeptide to a ligand and a labeled compound. **(IV)** Finally the patented claims of the '218 patent do not recite the assay temperature, while claim 22 recites the temperature of the screening assay between 1°C and 30°C. However, this limitation is inherent, because the specification of '218 discloses that the flashplate assay temperature should be between 1°C and 30°C (see column 7, lines 31-32). Additionally, optimization within prior art conditions or through routine experimentation is obvious to one skilled in the art. As stated in MPEP 2144.05:

"The differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages". *In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382; Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 UDPQ2d 1843 (Fed. Cir.).*

32. Therefore, the instant claims are not patentably distinct over the issued claims in U.S. patent 6,958,218.

Claim Rejections - 35 USC § 102

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

34. Claim 1,2 and 22 are rejected under 35 U.S.C. 102(a) as clearly anticipated by Brown and Gee (Jour Biol Chem. 273: 25458-25465, 1998 – cited by Applicant).

35. Claims 1, 2 and 22 are rejected under 35 U.S.C. 102(b) because Brown and Gee teach a method of screening of a ligand which binds to a cerebral cortical voltage-dependent calcium channel $\alpha_2\delta$ subunit, the method comprising the steps of contacting a secreted soluble recombinant calcium channel $\alpha_2\delta$ subunit polypeptide, Mutant L, with a ligand of interest and a labeled compound ([^{3}H] gabapentin) which binds the $\alpha_2\delta$ subunit at 22°C (page 25460, col. 1, lines 2-7; page 25462, columns 1 and 2; figure 2); and measuring the level of binding of the labeled compound to the $\alpha_2\delta$ subunit polypeptide (abstract, page 25461-miscellaneous methods). Brown and Gee refer to the subunit as '$\alpha_2\delta$'. However, as evidenced by Klugbauer et al (Jour Neuroscience 19: 684-691, 1999 – cited by Applicant), this subunit was later named as $\alpha_2\delta$-1 (Klugbauer, page 689), and is thus the same subunit referred to by the Applicant. Because the method steps disclosed by Brown and Gee meets the limitations of claims 1, 2, and 22 of the instant application, the method described in the reference anticipates the invention.

Claim Rejections - 35 USC § 103

36. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

37. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

38. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown and Gee (Jour Biol Chem. 273: 25458-25465, 1998), as applied to claims 1, 2 and 22 above, and further in view of Holland et al. (Anal Biochem. 222: 516-518, 1994).

39. Claim 4 recites a flashplate assay for the method of screening of ligands that bind to a recombinant soluble voltage-dependent calcium channel $\alpha_2\delta$-1 subunit.

40. The teachings of Brown and Gee are set forth above. Brown and Gee do not specifically teach a flashplate assay method.

41. Holland et al. teach a screening method of ligands using a flashplate assay wherein the contacting and binding is in the wells of a flashplate (see abstract), comprising the addition of the radioligand and test compound, incubation and measurement of the binding level.

42. It would have been obvious to the person of ordinary skill in the art at the time the claimed invention was made to screen for ligands that bind to the secreted soluble $\alpha_2\delta$-1 subunit of Brown and Gee, in the wells of a flashplate as taught by Holland et al. The person of ordinary skill in the art would have been motivated to use the flashplate technique for its simplicity and move towards automation and high-throughput screening assays (page 517, column 2). The person of ordinary skill in the art would have expected success because the method of screening of ligands using flashplate assay was well established in the art at the time the invention was made.

43. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

44. No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Rogawski MA and Loscher W Nature Med. 10: 685-692, 2004. (Reference showing the role of calcium channels in the binding of antiepileptic drugs)

Gee et al. (Jour Biol Chem. 271: 5768-5776, 1996) (Cross reference for method of screening of ligand).

45. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

46. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

47. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status

information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
August 25, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER